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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,120	06/14/2001	David Thomas Dudley	5968-01-SMH	5646
7590 07/20/2005 SUZANNE M. HARVEY WARNER-LAMBERT CO. 2800 PLYMOUTH ROAD ANN ARBOR, MI 48105			EXAMINER HUI, SAN MING R	
			ART UNIT 1617	PAPER NUMBER

DATE MAILED: 07/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/868,120

Applicant(s)

DUDLEY ET AL.

Examiner

San-ming Hui

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 6-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 6-16-05.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 4, 2005 has been entered. The addition of claims 24-28 is acknowledged.

Claims 6-28 are pending.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scherle et al. (The Journal of Immunology, 1998 Oct;161:5681-5686) and McGilvray et

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al. (The Journal of Biological Chemistry, 1997; 272(15): 10287-10294) in view of Robbins Pathologic basis of Disease, 5<sup>th</sup> ed., 1994, pages 1249-1253 and Bridges (WO 98/37881 from the International Search Report).

Scherle et al. teaches a MEK inhibitor, U0126, as effective in inhibiting the production of proinflammatory cytokines, such as IL-1, IL-8, TNF, and prostaglandin E2 (See the abstract and apge 5684, col. 2, first paragraph).

McGilvray et al. teaches the involvement of MAP kinase (MEK) pathway in the activation of monocytic cells during transmigration to inflammatory sites (See the abstract). McGilvray et al. teaches the selective inhibition of MAP kinase by MEK-1 inhibitor, PD98059, being useful for blocking and interrupting the adhesion and recruitments of human monocytes and thereby modulating the inflammatory response (See the abstract and page 10287, col. 2, second paragraph).

The primary references do not expressly teach the active compounds herein to be MEK inhibitors useful for the treatment of arthritis.

Robbins teaches several proinflammatroty mediators are involved in the pathogenesis of osteoarthritis and rheumatoid arthritis. And these proinflammatory mediators are IL-1, TNF- $\alpha$  (See pages 1247, 1251-1252 Pathogenesis Section).

Bridges teaches that the active compounds herein are MEK inhibitors (See page 3, line 16 – page 22, line 29). Bridges also teaches the specific MEK inhibitor recited in claim 17 herein as a preferred MEK inhibitor (See page 22, line 24-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis.

One of ordinary skill in the art would have been motivated to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis: the activation of MEK is known to be involved in reducing the inflammatory process, such as production of inflammatory cytokines and prostaglandin E2, interpretation of adhesion and recruitments of monocytes to the inflammatory sites, in the body. Furthermore, the inhibition of MEK is known to 1) suppress the production and release of pro-inflammatory cytokines such as interleukin-1 $\beta$ , PGE2, TNF, and interleukin-8, which are involved in the pathogenesis of both osteoarthritis and rheumatoid arthritis; and 2) block and interrupt the adhesion of monocytes to the inflammatory sites. Possessing the teachings of the prior art, the skilled artisan would therefore employ any known MEK inhibitors, including those MEK inhibitors of Bridges, to inhibit the production of the proinflammatory mediators and thereby treat arthritis such as rheumatoid arthritis and osteoarthritis, absent evidence to the contrary.

### ***Response to Arguments***

Applicant's arguments with respect to claims 6-28 have been considered but are moot in view of the new ground(s) of rejection.

The new ground of rejection has addressed the remarks raised by the applicant in the response filed May 4, 2005 because the proinflammatory mediators inhibited by

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MEK inhibitors are the ones which involve in the pathogenesis of osteoarthritis and that of rheumatoid arthritis. Therefore, possessing the teachings of the prior art, the skilled artisan would therefore employ any known MEK inhibitors, including those MEK inhibitors of Bridges, to inhibit the production of the proinflammatory mediators and thereby treat arthritis such as rheumatoid arthritis and osteoarthritis, absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
SAN-MING HUI  
PRIMARY EXAMINER

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San-ming Hui  
Primary Examiner  
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